

A FAMILIAL PARTIAL AZFb/c MICRODELETION ASSOCIATED WITH DIFFERENT FERTILE PHENOTYPES

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After the Klinefelter syndrome, Y chromosome microdeletions are the second most frequent genetic cause of spermatogenic failure resulting in male infertility. Y chromosome microdeletions, encompassing one or more of the three AZF regions, are associated with diverse testicular histology, ranging from Sertoli-cell-only syndrome (AZFa del), maturation arrest (AZFb del) to hypospermatogenesis (AZFc del). The molecular screening of these regions is routinely performed in the work-up of infertile patients with azoospermia or severe oligozoospermia as each one has different prognostic values, both in terms of clinical decision-making and appropriate genetic counselling as well as for understanding the etiology of spermatogenesis impairment. Different partial AZFc deletions were already described, although it is still controversial if these are truly a genetic risk factor for spermatogenesis impairment or a deletional variant without phenotypic consequences.

Here we present the molecular results obtained after AZF analysis of two infertile brothers (both diagnosed with oligoteratoastenozoospermia), and of their fertile father. Several multiplex-PCR assays were performed with distinct sets of STS markers, specific for the three AZF regions.

The molecular analysis revealed that all three men presented the same partial AZFb/c microdeletion, namely the absence of the sY1197, sY1291 and sY1192 STSs. This microdeletion probably results from the recombination of amplicons b1/b3, reducing the gene copy number of *PRY*, *BPY*, *DAZ*, and *RBMY*.

The b1/b3 deletion is rare and its influence on spermatogenesis is still not clear since it can be found in men with severe oligozoospermia or with normal sperm counts. Our result suggests that b1/b3 del is most likely a risk factor predisposing to spermatogenic failure, but is not sufficient alone. The different (in)fertile phenotypes associated with it, a fertile father opposed to his two infertile sons, can be possibly influenced by genetic background, environmental and epigenetic factors, contributing to different phenotypic expressions of individual/specific genomes.